



Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV

Downloaded from <https://aidsinfo.nih.gov/guidelines> on 1/18/2018

Visit the AIDSinfo website to access the most up-to-date guideline.

Register for e-mail notification of guideline updates at <https://aidsinfo.nih.gov/e-news>.

Drug-Resistance Testing (Last updated July 14, 2016; last reviewed July 14, 2016)

Panel's Recommendations

For Antiretroviral Therapy-Naïve Persons:

- HIV drug-resistance testing is recommended for persons with HIV at entry into care to guide selection of the initial antiretroviral therapy (ART) regimen **(AII)**. If therapy is deferred, repeat testing may be considered at the time of ART initiation **(CIII)**.
- Genotypic testing is recommended as the preferred resistance testing to guide therapy in antiretroviral (ARV)-naïve patients **(AIII)**.
- In special circumstances (e.g., in persons with acute or recent [early] HIV infection and in pregnant women with HIV), ART initiation should not be delayed while awaiting resistance testing results; the regimen can be modified once results are reported **(AIII)**.
- Standard genotypic drug-resistance testing in ARV-naïve persons involves testing for mutations in the reverse transcriptase (RT) and protease (PR) genes. If transmitted integrase strand transfer inhibitor (INSTI) resistance is a concern, providers should ensure that genotypic resistance testing also includes INSTI genotype testing **(BIII)**.

For Antiretroviral Therapy-Experienced Persons:

- HIV drug-resistance testing should be performed to assist in the selection of active drugs when changing ART regimens in the following patients:
 - In persons with virologic failure and HIV RNA levels >1,000 copies/mL **(AI)**.
 - In persons with HIV RNA levels >500 copies/mL but <1,000 copies/mL, drug-resistance testing may be unsuccessful but should still be considered **(BII)**.
 - Drug-resistance testing should also be performed when managing suboptimal viral load reduction **(AII)**.
- When a person with HIV experiences virologic failure while receiving an INSTI-based regimen, genotypic testing for INSTI resistance should be performed to determine whether to include a drug from this class in subsequent regimens **(AII)**.
- Drug-resistance testing in the setting of virologic failure should be performed while the person is taking prescribed ARV drugs or, if not possible, within 4 weeks after discontinuing therapy **(AII)**. If more than 4 weeks have elapsed since the ARVs were discontinued, resistance testing may still provide useful information to guide therapy; however, it is important to recognize that previously selected resistance mutations can be missed **(CIII)**.
- Genotypic testing is recommended as the preferred resistance testing to guide therapy in persons with suboptimal virologic response or virologic failure while on first- or second-line regimens **(AII)**.
- The addition of phenotypic to genotypic testing is generally preferred for persons with known or suspected complex drug-resistance mutation patterns **(BIII)**.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Co-Receptor Tropism Assays (Last updated February 12, 2013; last reviewed February 12, 2013)

Panel's Recommendations
<ul style="list-style-type: none">• A co-receptor tropism assay should be performed whenever the use of a CCR5 co-receptor antagonist is being considered (AI).• Co-receptor tropism testing is also recommended for patients with HIV who exhibit virologic failure while on a CCR5 antagonist (BIII).• A phenotypic tropism assay is preferred to determine HIV-1 co-receptor usage (AI).• A genotypic tropism assay should be considered as an alternative test to predict HIV-1 co-receptor usage (BII).
Rating of Recommendations: A = Strong; B = Moderate; C = Optional
Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

HLA-B*5701 Screening (Last updated December 1, 2007; last reviewed January 10, 2011)

Panel's Recommendations
<ul style="list-style-type: none">• The Panel recommends screening for HLA-B*5701 before starting patients on an abacavir (ABC)-containing regimen to reduce the risk of hypersensitivity reaction (HSR) (AI).• HLA-B*5701-positive patients should not be prescribed ABC (AI).• The positive status should be recorded as an ABC allergy in the patient's medical record (AI).• When HLA-B*5701 screening is not readily available, it remains reasonable to initiate ABC with appropriate clinical counseling and monitoring for any signs of HSR (CIII).
Rating of Recommendations: A = Strong; B = Moderate; C = Optional
Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Initiation of Antiretroviral Therapy (Last updated October 17, 2017; last reviewed October 17, 2017)

Panel's Recommendations
<ul style="list-style-type: none">• Antiretroviral therapy (ART) is recommended for all individuals with HIV, regardless of CD4 T lymphocyte cell count, to reduce the morbidity and mortality associated with HIV infection (AI).• ART is also recommended for individuals with HIV to prevent HIV transmission (AI).• When initiating ART, it is important to educate patients regarding the benefits and considerations of ART, and to address strategies to optimize adherence. On a case-by-case basis, ART may be deferred because of clinical and/or psychosocial factors, but therapy should be initiated as soon as possible.
Rating of Recommendations: A = Strong; B = Moderate; C = Optional
Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

What to Start: Initial Combination Regimens for the Antiretroviral-Naive Patient (Last updated October 17, 2017; last reviewed October 17, 2017)

Panel's Recommendations
<ul style="list-style-type: none"> An antiretroviral (ARV) regimen for a treatment-naive patient generally consists of two nucleoside reverse transcriptase inhibitors (NRTIs) in combination with a third active ARV drug from one of three drug classes: an integrase strand transfer inhibitor (INSTI), a non-nucleoside reverse transcriptase inhibitor (NNRTI), or a protease inhibitor (PI) with a pharmacokinetic (PK) enhancer (booster) (cobicistat or ritonavir). The Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) classifies the following regimens as Recommended Initial Regimens for Most People with HIV (in alphabetical order): <ul style="list-style-type: none"> Dolutegravir/abacavir/lamivudine^a—only for patients who are HLA-B*5701-negative (AI) Dolutegravir plus tenofovir/emtricitabine^{a,b} (AI) Elvitegravir/cobicistat/tenofovir/emtricitabine^b (AI) Raltegravir plus tenofovir/emtricitabine^{a,b} (AI for tenofovir disoproxil fumarate, AI for tenofovir alafenamide)^{a,b} To address individual patient characteristics and needs, the Panel also provides a list of Recommended Initial Regimens in Certain Clinical Situations (Table 6). Given the many excellent options for initial therapy, selection of a regimen for a particular patient should be guided by factors such as virologic efficacy, toxicity, pill burden, dosing frequency, drug-drug interaction potential, resistance testing results, comorbid conditions, access, and cost. Table 7 provides guidance on choosing an ARV regimen based on selected clinical case scenarios. Table 8 highlights the advantages and disadvantages of different components in a regimen.
<p>Rating of Recommendations: A = Strong; B = Moderate; C = Optional</p> <p>Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials, observational cohort studies with long-term clinical outcomes, relative bioavailability/bioequivalence studies, or regimen comparisons from randomized switch studies; III = Expert opinion</p>

^a Lamivudine may substitute for emtricitabine or vice versa.

^b Tenofovir alafenamide (TAF) and tenofovir disoproxil fumarate (TDF) are two forms of tenofovir approved by the Food and Drug Administration. TAF has fewer bone and kidney toxicities than TDF, while TDF is associated with lower lipid levels. Safety, cost, and access are among the factors to consider when choosing between these drugs.

Management of the Treatment-Experienced Patient

Virologic Failure (Last updated October 17, 2017; last reviewed October 17, 2017)

Panel's Recommendations

- Assessing and managing a patient experiencing failure of antiretroviral therapy (ART) is complex. Expert advice is critical and should be sought.
- Evaluation of virologic failure should include an assessment of adherence, drug-drug or drug-food interactions, drug tolerability, HIV RNA and CD4 T lymphocyte (CD4) cell count trends over time, ART history, and prior and current drug-resistance testing results.
- Drug-resistance testing should be performed while the patient is taking the failing antiretroviral (ARV) regimen (**AI**) or within 4 weeks of treatment discontinuation (**AII**). Even if more than 4 weeks have elapsed since ARVs were discontinued, resistance testing can still provide useful information to guide therapy, although it may not detect previously selected resistance mutations (**CIII**).
- The goal of treatment for ART-experienced patients with drug resistance who are experiencing virologic failure is to establish virologic suppression (i.e., HIV RNA below the lower limits of detection of currently used assays) (**AI**).
- A new regimen should include at least two, and preferably three, fully active agents (**AI**). A fully active agent is one that is expected to have uncompromised activity on the basis of the patient's ART history and his or her current and past drug-resistance testing results. A fully active agent may also have a novel mechanism of action.
- In general, adding a single ARV agent to a virologically failing regimen **is not recommended** because this may risk the development of resistance to all drugs in the regimen (**BII**).
- For some highly ART-experienced patients with extensive drug resistance, maximal virologic suppression may not be possible. In this case, ART should be continued (**AI**) with regimens designed to minimize toxicity, preserve CD4 cell counts, and delay clinical progression.
- When it is not possible to construct a viable suppressive regimen for a patient with multidrug resistant HIV, the clinician should consider enrolling the patient in a clinical trial of investigational agents or contacting pharmaceutical companies that may have investigational agents available.
- When switching an ARV regimen in a patient with hepatitis B virus (HBV)/HIV coinfection, ARV drugs active against HBV should be continued as part of the new regimen. Discontinuation of these drugs may cause serious hepatocellular damage resulting from reactivation of HBV.
- Discontinuing or briefly interrupting therapy may lead to a rapid increase in HIV RNA, a decrease in CD4 cell count, and an increase in the risk of clinical progression. Therefore, this strategy **is not recommended** in the setting of virologic failure (**AI**).
- Table 10 provides guidance on antiretroviral (ARV) regimen options in patients with virologic failure.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Poor CD4 Cell Recovery and Persistent Inflammation Despite Viral Suppression (Last updated April 8, 2015; last reviewed April 8, 2015)

Panel's Recommendations

- Morbidity and mortality from several AIDS and non-AIDS conditions are increased in individuals with HIV despite antiretroviral therapy (ART)-mediated viral suppression, and are predicted by persistently low CD4 T lymphocyte (CD4) cell counts and/or persistent immune activation.
- ART intensification by adding antiretroviral (ARV) drugs to a suppressive ART regimen does not consistently improve CD4 cell recovery or reduce immune activation and is not recommended **(AI)**.
- In individuals with viral suppression, switching ARV drug classes does not consistently improve CD4 cell recovery or reduce immune activation and is not recommended **(BIII)**.
- No interventions designed to increase CD4 cell counts and/or decrease immune activation are recommended at this time (in particular, interleukin-2 **is not recommended [AI]**) because no intervention has been proven to decrease morbidity or mortality during ART-mediated viral suppression.
- Monitoring markers of immune activation and inflammation **is not recommended** because no immunologically targeted intervention has proven to improve the health of individuals with abnormally high biomarker levels, and many markers that predict morbidity and mortality fluctuate widely in individuals **(AII)**.
- Because there are no proven interventions to improve CD4 cell recovery and/or inflammation, efforts should focus on addressing modifiable risk factors for chronic disease (e.g., encouraging smoking cessation, a healthy diet, and exercise; treating hypertension and hyperlipidemia) **(AII)**.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Regimen Switching in the Setting of Virologic Suppression (Last updated October 17, 2017; last reviewed October 17, 2017)

Panel's Recommendations

- Advances in antiretroviral (ARV) treatment and a better understanding of HIV drug resistance make it possible to consider switching an effective regimen to an alternative regimen in some situations.
- The fundamental principle of regimen switching is to maintain viral suppression without jeopardizing future treatment options **(AI)**.
- It is critical to review a patient's full ARV history, including virologic responses, past ARV-associated toxicities, and cumulative resistance test results (if available) before selecting a new antiretroviral therapy (ART) regimen **(AI)**.
- Adverse events, the availability of ARVs with an improved safety profile, or the desire to simplify a regimen may prompt a regimen switch. Within-class and between-class switches can usually maintain viral suppression, provided that there is no viral resistance to the ARV agents in the new regimen **(AI)**.
- Monotherapy with either a boosted protease inhibitor (PI) or an integrase strand transfer inhibitor (INSTI) has been explored in several trials or cohort studies, and has been associated with an unacceptable rate of virologic failure and the development of resistance; therefore, monotherapy as a switching strategy **is not recommended (AII)**.
- When switching an ARV regimen in a patient with hepatitis B virus (HBV)/HIV coinfection, ARV drugs active against HBV infection should be continued as part of the new regimen. Discontinuation of these drugs may cause serious hepatocellular damage resulting from reactivation of HBV.
- Consultation with an HIV specialist should be considered when planning a regimen switch for a patient with a history of resistance to one or more drug classes **(BIII)**.
- More intensive monitoring to assess tolerability, viral suppression, adherence, and laboratory changes is recommended during the first 3 months after a regimen switch **(AIII)**.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Exposure-Response Relationship and Therapeutic Drug Monitoring (TDM) for Antiretroviral Agents (Last updated April 8, 2015; last reviewed April 8, 2015)

Panel's Recommendations

- Therapeutic drug monitoring (TDM) for antiretroviral agents is not recommended for routine use in the management of patients with HIV **(BII)**.
- TDM may be considered in selected clinical scenarios, as discussed in the text below.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Considerations for Antiretroviral Use in Special Patient Populations

Acute and Recent (Early^a) HIV Infection (Last updated October 17, 2017; last reviewed October 17, 2017)

Panel's Recommendations

- Antiretroviral therapy (ART) is recommended for all individuals with HIV-1 infection (**AI**) including those with early^a HIV-1 infection.
- Once initiated, the goal of ART is to suppress plasma HIV-1 RNA to undetectable levels (**AIII**). Testing for plasma HIV-1 RNA levels, CD4 T lymphocyte counts, and toxicity monitoring should be performed as recommended for patients with chronic HIV-1 infection (**AII**).
- Genotypic drug resistance testing should be performed before initiation of ART to guide the selection of the regimen (**AII**).
- ART can be initiated before drug resistance test results are available. Because resistance to pharmacokinetically enhanced protease inhibitors (PIs) emerges slowly and clinically significant transmitted resistance to PIs is uncommon, a boosted darunavir (DRV) and emtricitabine (FTC) plus either tenofovir disoproxil fumarate (TDF) or tenofovir alafenamide (TAF) are recommended regimens in this setting (**AIII**). For similar reasons, dolutegravir (DTG) and FTC plus either TDF or TAF are also reasonable options, although data regarding transmission of integrase strand transfer inhibitor (INSTI)-resistant HIV and the efficacy of DTG regimens in early HIV infection is more limited (**AIII**).
- When results of drug resistance testing are available, the treatment regimen can be modified if warranted (**AII**). In patients without transmitted drug resistant virus, therapy should be initiated with one of the combination regimens that is recommended for patients with chronic HIV-1 infection (see [What to Start](#)) (**AIII**).
- Patients starting ART should be willing and able to commit to treatment and should understand the importance of adherence (**AIII**). Patients may choose to postpone therapy, and providers, on a case-by-case basis, may recommend that patients defer therapy because of clinical or psychosocial factors.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

^a Early infection represents either acute or recent infection.

Adolescents and Young Adults with HIV (Last updated January 28, 2016; last reviewed January 28, 2016)

Key Summary and Panel's Recommendations

- Adolescents living with HIV largely belong to two distinct groups—those who acquired HIV in infancy, and are heavily antiretroviral therapy (ART)-experienced, and those who acquired HIV more recently during their teens.
- ART is recommended for all individuals with HIV **(AI)** to reduce morbidity and mortality. Thus, ART is also recommended for ART-naïve adolescents. However, before initiation of therapy, adolescents' readiness and ability to adhere to therapy within their psychosocial context need to be carefully considered as part of therapeutic decision making **(AIII)**.
- Once ART is initiated, appropriate support is essential to reduce potential barriers to adherence and maximize the success in achieving sustained viral suppression **(AII)**.
- The adolescent sexual maturity rating can be helpful to guide regimen selection for initiation of or changes in ART as recommended by either these Adult and Adolescent ARV Guidelines or the Pediatric ARV Guidelines. These Adult/Adolescent Guidelines are more appropriate for postpubertal adolescents (i.e., sexual maturity rating IV or V) **(AIII)**.
- Pediatric and adolescent care providers should prepare adolescents for the transition into adult care settings. Adult providers should be sensitive to the challenges associated with such transitions, consulting and collaborating with adolescent HIV care providers to insure adolescents' successful transition and continued engagement in care **(AIII)**.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Women with HIV (Last updated July 14, 2016; last reviewed July 14, 2016)

Panel's Recommendations

- Antiretroviral therapy (ART) is recommended for all women living with HIV to improve their health and to reduce the risk of HIV transmission to HIV-uninfected sex partners **(AI)**.
- In pregnant women, an additional goal of therapy is to maintain a viral load below the limit of detection throughout pregnancy to reduce the risk of transmission to the fetus and newborn **(AI)**.
- When selecting an antiretroviral (ARV) combination regimen for a pregnant woman, clinicians should consider the available safety, efficacy, and pharmacokinetic (PK) data on use during pregnancy for each agent. The risks and benefits of ARV use during pregnancy should be discussed with all women **(AIII)**.
- For women taking ARV drugs that have significant PK interactions with hormonal contraceptives, an alternative or additional effective contraceptive method to prevent unintended pregnancy is recommended **(AIII)**. Switching to an ARV drug without interactions with hormonal contraceptives may also be considered **(BIII)**.
- Nonpregnant women of childbearing potential should undergo pregnancy testing before initiation of efavirenz (EFV) and receive counseling about the potential risk to the fetus and desirability of avoiding conception while on EFV-based regimens **(AIII)**.
- When designing a regimen for a pregnant woman, clinicians should consult the most current [Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States \(Perinatal Guidelines\)](#) **(AIII)**.
- Regimens that do not include EFV should be considered in women who are planning to become pregnant or are sexually active and not using effective contraception **(BIII)**.
- Women on a suppressive regimen containing EFV who become pregnant and present to antenatal care during the first trimester can continue EFV throughout pregnancy **(CIII)**.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

HIV-2 Infection (Last updated April 8, 2015; last reviewed April 8, 2015)

Summary of HIV-2 Infection

- Compared to HIV-1 infection, the clinical course of HIV-2 infection is generally characterized by a longer asymptomatic stage, lower plasma HIV-2 RNA levels, and lower mortality; however, progression to AIDS does occur.
- There have been no randomized trials addressing the question of when to start antiretroviral therapy (ART) or the choice of initial or second-line therapy for HIV-2 infection; thus, the optimal treatment strategy has not been defined.
- Although the optimal CD4 T lymphocyte (CD4) cell count threshold for initiating ART in HIV-2 infection is unknown, therapy should be started before there is clinical progression.
- HIV-2 is intrinsically resistant to non-nucleoside reverse transcriptase inhibitors and to enfuvirtide; thus, these drugs should not be included in an antiretroviral regimen for a patient living with HIV-2 infection.
- Pending more definitive data on outcomes in an ART-naïve patient who has HIV-2 mono-infection or HIV-1/HIV-2 dual infection and requires treatment, an initial antiretroviral therapy regimen for these patients should include two nucleoside reverse transcriptase inhibitors plus an HIV-2 active boosted protease inhibitor or integrase strand transfer inhibitors.
- A few laboratories now offer quantitative plasma HIV-2 RNA testing for clinical care (see section text).
- Monitoring of HIV-2 RNA levels, CD4 cell counts, and clinical improvements can be used to assess treatment response, as is recommended for HIV-1 infection.
- Resistance-associated viral mutations to nucleoside reverse transcriptase inhibitors, protease inhibitors, and/or integrase strand transfer inhibitors may develop in patients with HIV-2 while on therapy. However, no validated HIV-2 genotypic or phenotypic antiretroviral resistance assays are available for clinical use.
- In the event of virologic, immunologic, or clinical failure, second-line treatment should be instituted in consultation with an expert in HIV-2 management.

HIV and the Older Patient (Last updated January 28, 2016; last reviewed January 28, 2016)

Key Considerations When Caring for Older Patients With HIV

- Antiretroviral therapy (ART) is recommended for all patients regardless of CD4 T lymphocyte cell count (**AI**). ART is especially important for older patients because they have a greater risk of serious non-AIDS complications and potentially a blunted immunologic response to ART.
- Adverse drug events from ART and concomitant drugs may occur more frequently in older patients living with HIV than in younger patients with HIV. Therefore, the bone, kidney, metabolic, cardiovascular, and liver health of older patients should be monitored closely.
- Polypharmacy is common in older patients with HIV; therefore, there is a greater risk of drug-drug interactions between antiretroviral drugs and concomitant medications. Potential for drug-drug interactions should be assessed regularly, especially when starting or switching ART and concomitant medications.
- HIV experts, primary care providers, and other specialists should work together to optimize the medical care of older patients with HIV with complex comorbidities.
- Early diagnosis of HIV and counseling to prevent secondary transmission of HIV remains an important aspect of the care of the older patient with HIV.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Considerations for Antiretroviral Use in Patients with Coinfections

Hepatitis B/HIV Virus Coinfection (Last updated October 17, 2017; last reviewed October 17, 2017)

Panel's Recommendations

- Before initiation of antiretroviral therapy (ART), all patients who test positive for hepatitis B surface antigen (HBsAg) should be tested for hepatitis B virus (HBV) DNA using a quantitative assay to determine the level of HBV replication (**AIII**).
- Because emtricitabine (FTC), lamivudine (3TC), tenofovir disoproxil fumarate (TDF), and tenofovir alafenamide (TAF) have activity against both HIV and HBV, an ART regimen for patients with both HIV and HBV should include (TAF or TDF) plus (3TC or FTC) as the nucleoside reverse transcriptase inhibitor (NRTI) backbone of a fully suppressive antiretroviral (ARV) regimen (**AI**).
- If TDF or TAF cannot safely be used, the alternative recommended HBV therapy is entecavir in addition to a fully suppressive ARV regimen (**BI**). Entecavir has activity against HIV; its use for HBV treatment without ART in patients with dual infection may result in the selection of the M184V mutation that confers HIV resistance to 3TC and FTC. Therefore, entecavir must be used in addition to a fully suppressive ARV regimen when given to patients with HBV/HIV-coinfection (**AII**). Peginterferon alfa monotherapy may also be considered in certain patients (**CII**).
- Other HBV treatment regimens, including adefovir alone or in combination with 3TC or FTC and telbivudine, **are not recommended** for patients with HBV/HIV coinfection (**CII**).
- Discontinuation of agents with anti-HBV activity may cause serious hepatocellular damage resulting from reactivation of HBV; patients should be advised against stopping these medications and be carefully monitored during interruptions in HBV treatment (**AII**).
- If ART needs to be modified due to HIV virologic failure and the patient has adequate HBV suppression, the ARV drugs active against HBV should be continued for HBV treatment in combination with other suitable ARV agents to achieve HIV suppression (**AIII**).
- HBV reactivation has been observed in persons with HBV infection during interferon-free HCV treatment. For that reason, all patients initiating HCV therapy should be tested for HBV. Persons with HCV/HIV coinfection and active HBV infection (determined by a positive HBsAg test) should receive ART that includes two agents with anti-HBV activity prior to initiating HCV therapy (**AIII**).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Panel's Recommendations

- All people with HIV should be screened for hepatitis C virus (HCV) infection (**AIII**). Patients at high risk of HCV infection should be screened annually and whenever incident HCV infection is suspected (**AIII**).
- Antiretroviral therapy (ART) may slow the progression of liver disease by preserving or restoring immune function and reducing HIV-related immune activation and inflammation. For most persons with HCV/HIV coinfection, including those with cirrhosis, the benefits of ART outweigh concerns regarding drug-induced liver injury. Therefore, ART should be initiated in all patients with HCV/HIV coinfection, regardless of CD4 T lymphocyte (CD4) cell count (**AI**).
- Initial ART regimens recommended for most patients with HCV/HIV coinfection are the same as those recommended for individuals without HCV infection. However, when treatment for both HIV and HCV is indicated, the ART and HCV treatment regimen should be selected with special consideration for potential drug-drug interactions and overlapping toxicities (see discussion in the text below and in [Table 12](#)).
- In patients with lower CD4 counts (e.g., <200 cells/mm³), ART should be initiated promptly (**AI**) and HCV therapy may be delayed until the patient is stable on HIV treatment (**CIII**).
- All patients with HCV/HIV coinfection should be evaluated for HCV therapy and have their liver fibrosis stage assessed to inform the length of their therapy, ribavirin need (a concern with some regimens), and subsequent risk of hepatocellular carcinoma and liver disease complications.
- Persons with chronic HCV/HIV coinfection should be screened for active and prior hepatitis B virus (HBV) infection by testing for the presence of hepatitis B surface antigen (HBsAg) and antibodies to hepatitis B surface (HBsAb) and core (HBcAb total or IgG). Persons who are not immune to HBV infection (HBsAb-negative) should receive anti-HBV vaccination (**AIII**).
- HBV reactivation has been observed in persons with HBV infection during interferon-free HCV treatment. Accordingly, persons with HCV/HIV coinfection and active HBV infection (HBsAg-positive) should receive ART that includes two agents with anti-HBV activity prior to initiating HCV therapy (**AIII**).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Tuberculosis/HIV Coinfection (Last updated July 14, 2016; last reviewed July 14, 2016)

Panel's Recommendations

- Selection of a tuberculosis (TB)-preventive treatment for individuals living with HIV and coinfecting with latent tuberculosis infection (LTBI) should be based on the individual's antiretroviral therapy (ART) regimen as noted below:
 - Any ART regimen can be used when isoniazid alone is used for LTBI treatment **(AII)**.
 - Only efavirenz (EFV)- or raltegravir (RAL)-based regimens (in combination with either abacavir/lamivudine [ABC/3TC] or tenofovir disoproxil fumarate/emtricitabine [TDF/FTC]) can be used with once-weekly isoniazid plus rifapentine **(AIII)**.
 - If rifampin or rifabutin is used to treat LTBI, clinicians should review [Tables 18a through 18e](#) to assess the potential for interactions among different antiretroviral (ARV) drugs and the rifamycins **(BIII)**.
- All patients with both HIV and active TB who are not on ART should be started on ART as described below:
 - **In patients with CD4 counts <50 cells/mm³:** Initiate ART as soon as possible, but within 2 weeks of starting TB treatment **(AI)**.
 - **In patients with CD4 counts ≥50 cells/mm³:** Initiate ART within 8 weeks of starting TB treatment **(AIII)**.
 - **In all pregnant women with HIV:** Initiate ART as early as feasible, for treatment of maternal HIV infection and to prevent mother-to-child transmission (MTCT) of HIV **(AIII)**.
 - **In patients with tuberculous meningitis:** Caution should be exercised when initiating ART early, as high rates of adverse events and deaths have been reported in a randomized trial **(AI)**.
- Rifamycins are critical components of TB treatment regimens and should be included for patients with both HIV and active TB, unless precluded because of TB resistance or toxicity. However, rifamycins have a considerable potential for drug-drug interactions. Clinicians should review [Tables 18a through 18e](#) to assess the potential for interactions among different ARV drugs and the rifamycins **(BIII)**.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Limitations to Treatment Safety and Efficacy

Adherence to the Continuum of Care (Last reviewed October 17, 2017)

Key Summary of Adherence to the Continuum of Care

- Linkage-to-care and adherence to both antiretroviral therapy (ART) and clinic appointments should be regularly assessed.
- An individual's barriers to adherence to ART and appointments should be assessed before initiation of ART and regularly thereafter.
- Patients with ART adherence problems should be placed on regimens with high genetic barriers to resistance, such as dolutegravir (DTG) or boosted darunavir (DRV). Side effects, out-of-pocket costs, convenience, and patient preferences also need to be considered.
- Patients having difficulties with adherence to appointments or ART should be approached in a constructive, collaborative, nonjudgmental, and problem-solving manner.
- The approach to improved adherence should be tailored to each person's needs (or barriers to care). Approaches could include, but are not limited to:
 - Changing ART to simplify dosing or reduce side effects
 - Finding resources to assist with treatment costs to maintain uninterrupted access to both ART and appointments
 - Allowing flexible appointment scheduling
 - Assisting with transportation, or
 - Linking patients to counseling to overcome stigma, substance use, or depression.
- Multidisciplinary approaches to find solutions to ART and appointment adherence problems are often necessary, including collaboration with social work and case management (to the extent available). The clinician's role is to help the patient understand the importance of adherence to the continuum of care and reveal barriers to adherence, and link the patient to resources to overcome those barriers.
- A summary of best practice interventions to improve linkage, retention, and adherence can be found at a Centers for Disease Control and Prevention compendium (<https://www.cdc.gov/hiv/research/interventionresearch/compendium/index.html>).